

**Listing of Claims:**

1. (Currently amended) An imaging agent which comprises a synthetic barbituric acid matrix metalloproteinase inhibitor labelled at the 5-position of the barbituric acid with an imaging moiety, wherein the imaging moiety can be detected externally in a non-invasive manner following administration of said labelled synthetic barbituric acid matrix metalloproteinase inhibitor to the mammalian body *in vivo*, and said imaging moiety is chosen from:
  - (i) a radioactive metal ion;
  - (ii) a paramagnetic metal ion;
  - (iii) a gamma-emitting radioactive halogen;
  - (iv) a positron-emitting radioactive non-metal;
  - (v) a hyperpolarised NMR-active nucleus;
  - (vi) a reporter suitable for *in vivo* optical imaging;
  - (vii) ~~a  $\beta$ -emitter suitable for intravascular detection.~~
2. (Original) The imaging agent of Claim 1, where the synthetic barbituric acid matrix metalloproteinase inhibitor ligand conjugate is of Formula I:

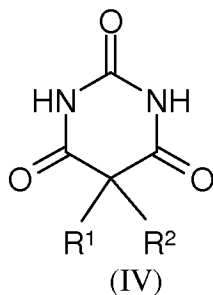


where:

{inhibitor} is the synthetic barbituric acid matrix metalloproteinase inhibitor;  
-(A)<sub>n</sub>- is a linker group wherein each A is independently -CR<sub>2</sub>-, -CR=CR-, -C≡C-, -CR<sub>2</sub>CO<sub>2</sub>-, -CO<sub>2</sub>CR<sub>2</sub>-, -NRCO-, -CONR-, -NR(C=O)NR-, -NR(C=S)NR-, -SO<sub>2</sub>NR-, -NRSO<sub>2</sub>-, -CR<sub>2</sub>OCR<sub>2</sub>-, -CR<sub>2</sub>SCR<sub>2</sub>-, -CR<sub>2</sub>NRCR<sub>2</sub>-, a C<sub>4-8</sub> cycloheteroalkylene group, a C<sub>4-8</sub> cycloalkylene group, a C<sub>5-12</sub> arylene group, or a C<sub>3-12</sub> heteroarylene group, an amino acid or a monodisperse polyethyleneglycol (PEG) building block;  
R is independently chosen from H, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl,

C<sub>1-4</sub> alkoxyalkyl or C<sub>1-4</sub> hydroxyalkyl;  
n is an integer of value 0 to 10; and  
m is 1, 2 or 3.

3. (Previously presented) The imaging agent of Claim 1, where the synthetic barbituric acid matrix metalloproteinase inhibitor is conjugated to a ligand, and said ligand forms a metal complex with the radioactive metal ion or paramagnetic metal ion.
4. (Original) The imaging agent of Claim 3, where the ligand is a chelating agent.
5. (Previously presented) The imaging agent of Claim 3, where the radioactive metal ion is a gamma emitter or a positron emitter.
6. (Original) The imaging agent of Claim 5, where the radioactive metal ion is <sup>99m</sup>Tc, <sup>111</sup>In, <sup>64</sup>Cu, <sup>67</sup>Cu, <sup>67</sup>Ga or <sup>68</sup>Ga.
7. ((Previously presented) The imaging agent of Claim 1, where the gamma-emitting radioactive halogen imaging moiety is <sup>123</sup>I.
8. (Previously presented) The imaging agent of Claim 1, where the positron-emitting radioactive non-metal is chosen from <sup>18</sup>F, <sup>11</sup>C or <sup>13</sup>N.
9. (Previously presented) The imaging agent of Claim 1, where the synthetic barbituric acid matrix metalloproteinase inhibitor is of Formula IV:



where:

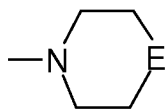
R<sup>1</sup> is R" or a Z group;

$R^2$  is  $R''$ , Y or  $-NR^4R^5$ , where  $R^4$  is H or an  $R''$  group,  $R^5$  is H,  $C_{2-14}$  acyl,  $C_{2-10}$  aminoalkyl or (N- $C_{2-14}$  acyl) $C_{2-10}$  aminoalkyl or an  $R''$  group, or  $R^4$  and  $R^5$  together with the N atom to which they are attached form an optionally (N- $C_{2-14}$ )acylated  $C_{2-8}$  cycloaminoalkylene ring;

$R''$  is independently  $C_{1-14}$  alkyl,  $C_{3-8}$  cycloalkyl,  $C_{2-14}$  alkenyl,  $C_{1-14}$  fluoroalkyl,  $C_{1-14}$  perfluoroalkyl,  $C_{6-14}$  aryl,  $C_{2-14}$  heteroaryl or  $C_{7-16}$  alkylaryl;

Z is a group of formula  $-A^1O[A^2O]_pR^3$  where p is 0 or 1, and  $A^1$  and  $A^2$  are independently  $C_{1-10}$  alkylene,  $C_{3-8}$  cycloalkylene,  $C_{1-10}$  perfluoroalkylene,  $C_{6-10}$  arylene or  $C_{2-10}$  heteroarylene, and  $R^3$  is an R group where R is independently chosen from H,  $C_{1-4}$  alkyl,  $C_{2-4}$  alkenyl,  $C_{2-4}$  alkynyl,  $C_{1-4}$  alkoxyalkyl or  $C_{1-4}$  hydroxyalkyl;

Y is a group of formula:

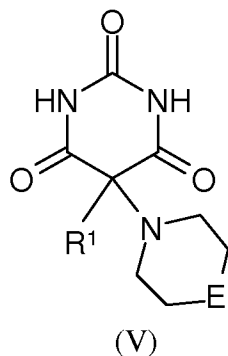


where E is  $CR_2$ , O, S or  $NR^6$ ; and  $R^6$  is  $C_{2-14}$  acyl, or an  $R''$  or Z group.

10. (Original) The imaging agent of claim 9, where  $R^2$  is Y or  $-NR^4R^5$ .

11. (Previously presented) The imaging agent of claim 9, where the imaging moiety is attached to the  $R^2$  substituent.

12. (Previously presented) The imaging agent of claim 9, of Formula V:



where E is CHR or NR<sup>6</sup> and R<sup>1</sup> is C<sub>6-14</sub> *n*-alkyl, or C<sub>6-14</sub> aryl.

13. (Original) The imaging agent of claim 12, where E is NR<sup>6</sup> and R<sup>6</sup> is C<sub>2-14</sub> acyl; -(CH<sub>2</sub>)<sub>d</sub>OH, where d is 2, 3, 4 or 5; or -C<sub>6</sub>H<sub>4</sub>X, where X is H, C<sub>1-4</sub> alkyl, Hal, OR, NR<sub>2</sub>, NO<sub>2</sub> or SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, where R<sup>7</sup> and R<sup>8</sup> are independently R groups, and R is as defined in Claim 9.
14. (Previously presented) The imaging agent of claim 12, where R<sup>1</sup> is *n*-octyl, *n*-decyl, biphenyl, C<sub>6</sub>H<sub>5</sub>X or -C<sub>6</sub>H<sub>4</sub>-O-C<sub>6</sub>H<sub>4</sub>X where X is as defined in Claim 13.
15. (Previously presented) A pharmaceutical composition which comprises the imaging agent of claim 1 together with a biocompatible carrier, in a form suitable for mammalian administration.
16. (Previously presented) A radiopharmaceutical composition which comprises the imaging agent of claim 1 wherein the imaging moiety is radioactive, together with a biocompatible carrier, in a form suitable for mammalian administration.
17. (Original) The radiopharmaceutical composition of claim 16, where the imaging moiety comprises a radioactive metal ion.
18. (Original) The radiopharmaceutical composition of claim 16, where the imaging moiety comprises a positron-emitting radioactive non-metal or a gamma-emitting radioactive halogen.
19. (Original) A conjugate of a synthetic barbituric acid matrix metalloproteinase inhibitor with a ligand, wherein the barbituric acid comprises a 5-position substituent, and said 5-position substituent comprises a ligand capable of forming a metal complex with a radioactive or paramagnetic metal ion which is resistant to transchelation.
20. Original) The conjugate of Claim 19, of Formula Ib:



where {inhibitor}, A, n and m are as defined in Claim 2.

21. (Previously presented) The conjugate of Claim 19, wherein the synthetic barbituric acid matrix metalloproteinase inhibitor is of Formula IV or Formula V of Claims 9 to 14.
22. (Previously presented) The conjugate of Claim 19, wherein the ligand is a chelating agent.
23. (Original) The conjugate of Claim 22, wherein the chelating agent has a diaminedioxime,  $\text{N}_2\text{S}_2$ , or  $\text{N}_3\text{S}$  donor set.
24. (Previously presented) A kit for the preparation of the radiopharmaceutical composition of Claim 17, which comprises a conjugate of a synthetic barbituric acid matrix metalloproteinase inhibitor with a ligand, wherein the barbituric acid comprises a 5-position substituent, and said 5-position substituent comprises a ligand capable of forming a metal complex with a radioactive or paramagnetic metal ion which is resistant to transchelation, said conjugate being of Formula Ib:
- $$[\{\text{inhibitor}\}-(A)_n]_m\text{-[ligand]} \quad (\text{Ib}),$$
- where {inhibitor}, A, n and m are as defined in Claim 2, and wherein the ligand is a chelating agent.
25. (Original) The kit of Claim 26, where the radioactive metal ion is  $^{99\text{m}}\text{Tc}$ , and the kit further comprises a biocompatible reductant.
26. (Previously presented) A kit for the preparation of the radiopharmaceutical composition of Claim 18, which comprises a precursor in sterile form which is a non-radioactive derivative of the barbituric acid matrix metalloproteinase inhibitor of claims 1, wherein

said non-radioactive derivative is capable of reaction with a source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen to give the desired radiopharmaceutical.

27. (Original) The kit of Claim 26, where the source of the positron-emitting radioactive non-metal or gamma-emitting radioactive halogen is chosen from:

- (i) halide ion;
- (ii)  $F^+$  or  $I^+$ ; or
- (iii) an alkylating agent chosen from an alkyl or fluoroalkyl halide, tosylate, triflate or mesylate;
- (iv)  $HS(CH_2)_3^{18}F$ .

28. (Previously presented) The kit of claim 26, wherein the non-radioactive derivative is chosen from:

- (i) an organometallic derivative such as a trialkylstannane or a trialkylsilane;
- (ii) a derivative containing an alkyl or aryl iodide or bromide, alkyl tosylate or alkyl mesylate for nucleophilic substitution;
- (iii) a derivative containing an aromatic ring activated towards nucleophilic or electrophilic substitution;
- (iv) a derivative containing a functional group which undergoes facile alkylation;
- (v) a derivative which undergoes alkylation with an alkyl thiol to give a thioether.

29. (Previously presented) The kit of claim 26, where the precursor is bound to a solid phase.

30. (Previously presented) Use of the imaging agent of Claim 1 for the diagnostic imaging of atherosclerosis.

31. (Previously presented) Use of the imaging agent of Claim 1 for the diagnostic imaging of unstable plaques.

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32. (Previously presented) Use of the imaging agent of Claim 1 for the intravascular detection of atherosclerosis.